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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/623,737	09/07/00	DOBRUSIN	E 5716-01-CA

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EXAMINER	
TRUONG, T	
ART UNIT	**PAPER NUMBER**
1624	4

DATE MAILED: 02/16/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/623,737	DOBRUSIN ET AL.	
	Examiner	Art Unit	
	Tamthom N. Truong	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-43* is/are pending in the application.

4a) Of the above claim(s) *17-24* is/are withdrawn from consideration.

5)☒ Claim(s) *9, 11, 13, 16, and 42* is/are allowed.

6)☒ Claim(s) *1, 2, 7, 8, 10, 12, 15, 25-41, and 43* is/are rejected.

7)☒ Claim(s) *3-6, and 14* is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15)☒ Notice of References Cited (PTO-892)
16)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3 .
18)☐ Interview Summary (PTO-413) Paper No(s). _____ .
19)☐ Notice of Informal Patent Application (PTO-152)
20)☐ Other: .

DETAILED ACTION

LACK OF UNITY

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 C.F.R 1.499, applicants are required, in response to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 1 (in part), 2-16, and 25-43(in part), drawn to compounds, compositions and methods of using formula I wherein both of G and Z are nitrogen (N) atoms.

Group II, claim(s) 1 (in part), 17-24, 25-41 (in part), and 43 (in part), drawn to compounds, compositions and methods of using formula I wherein either G or Z is nitrogen (N) atom, and the other is –CH-.

Group III, claim(s) 1 (in part), 25-41 (in part), and 43 (in part), drawn to compounds, compositions and methods of using formula I wherein both G and Z are –CH-.

The inventions listed as Groups I to III do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

A. All of the groupings are directed to a bicyclic derivative of formula I, but each group has a different special technical feature not shared by the remaining groups. That is, Group I is directed to derivatives of **pyrimido[4,5-d]pyrimidin-2(1H)-one**, or **3,4-dihydro- pyrimido[4,5-d]pyrimidin-2(1H)-one** (or bicycle with 4 N's) which is the special technical feature not shared by the remaining two groups. Likewise, Group II is directed to derivatives of **8H-pyrido[4,3-d]pyrimidin-7-one**, or **3,4-dihydro-pyrido[4,3-d]pyrimidin-2(1H)-one** (or bicycle with 3 N's) which is the special technical feature not shared by Groups I and III. Finally, Group III is directed to derivatives of **pyrido-pyridinone** (or bicycle with 2 N's) which is the special technical feature not shared by the above groups.

B. Although groups I to III share a special technical feature(s) of W-R^1, said special technical feature(s) does not define a contribution over the prior art, i.e., it can be anticipated by or obvious in view of the prior art.

C. Under 35 U.S.C. 372(b)(2), "international applications designating but not originating in, the United States...the Commissioner may cause the question of unity of invention to be reexamined under section 121 of this title..." Thus, as discussed above, the instant invention clearly lacks unity according to PCT 13.2. Accordingly, restriction under 35 U.S.C. 121 and 372 is deemed necessary.

During a telephone conversation with Mr. Charles Ashbrook on 2-5-01 a provisional election was made with traverse to prosecute the invention of Group I, claims 1 (in part), 2-16, and 25-43 (in part). Affirmation of this election must be made by applicant in replying to this Office action. Claims 17-24 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicants are advised that the reply to this requirement to be complete must include an election of the invention to be examined (37 C.F.R 1.143).

Applicants are reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 C.F.R 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 C.F.R 1.48(b) and by the fee required under 37 C.F.R 1.17(I).

1. **Improper Markush**: Claims 1, and 25-41, and 43 are rejected on the ground of Judicially Created Doctrine as being drawn to Improper Markush Groups. **In re Harnisch**, 206 USPQ 300. The recited compounds, while possessing a common utility present a variable core, and thus the Markush Groups represented by the terms "G" and "Z" render the claims clearly improper.

Specification

2. **Abstract:** This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required. Applicant is reminded of the proper content of an Abstract of the Disclosure.

In chemical patent abstracts for compounds or compositions, the general nature of the compound or composition should be given as well as its use, *e.g.*, "The compounds are of the class of alkyl benzene sulfonyl ureas, useful as oral anti-diabetics." Exemplification of a species could be illustrative of members of the class. For processes, the type reaction, reagents and process conditions should be stated, generally illustrated by a single example unless variations are necessary.

3. The disclosure is objected for the following discrepancies:

- Page 32, the formula with $-NHR^{10}$ is inconsistent with formula I wherein X is NR^{10};
- Page 37, the final product in Scheme 1c is inconsistent with formula I;
- Pages 40 and 41, the formula with G as –N= is inconsistent with formula I.

Appropriate correction is requested.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1, 10, 12, 15, 25, 26, 30, and 34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

a. Claims 1, 25, 26, 30, and 34 recite the following limitations which are ambiguous:

i. The definitions of R^1, R^2, R^{10}, T, and Q include functional groups such as: $N(O)R^4R^5$; $N(O)R^4$; $N(O)R^5$; $NR^4R^5R^6Y$; NR^4R^6Y; NR^5R^6Y. The N atom in said groups must have a positive charge, and cannot be neutral as recited.

ii. The definition of R^9 calls for a "carbonyl", "thiocarbonyl", or "imine" group when the dotted line is absent. However, said functional groups have incomplete valence. Thus, it is unclear as to what terminal groups for them are.

b. Claims 10 and 12 lack antecedent basis because they recite compounds with –$NHC(=O)-R^4$ at the position of X, which is not the same compound of formula I when X is NR^{10} as recited in claim 1.

c. Claim 15 lacks antecedent basis because it recites a compound with two oxo groups which is not recited in claim 1.

Claim Rejections - 35 USC § 101and 112, first paragraph

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4. Claims 25-36, 38, 40, and 41are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either an asserted utility or a well-established utility. A revised utility guideline requires that utilities must be specific, substantial, and credible.

By specific, said guidelines call for a particular disorder or disease. In the case of cancer treatment, a specific type of cancer must be indicated. By substantial, said guidelines require that utilities must define a "real world" use, and must not constitute further research to identify or reasonably confirm a "real world" context of use. In the instant case, said claims call for the following non-specific and unsubstantial utilities:

- Treatment of cancer (without specific types of cancer named);
- Inhibiting a cyclin-dependent kinase;
- Inhibiting growth factor mediated tyrosine kinase;
- Inhibiting non-receptor tyrosine kinase;
- Inhibiting serine kinase, and
- Inhibiting wee-1 kinase enzyme.

Note, the specification does not appear to relate a specfic disorder to said methods. Furthermore, said methods are not well known methods, and thus require extensive further research. Because applicant has not disclosed any specific and substantial utility for the claimed invention, credibility will not be assessed. See **Brenner v. Manson**, 148 USPQ 689, and **In re Zeigler**, 26 USPQ 2d 1600, 1603 (Fed. Cir. 1996).

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 25-36, 38, 40 and 41 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. Given the complication of treating cancers and inhibiting various kinases (without interfering the function of each other), one skilled in the art would not have known how to treat said cancers and disorders related to various kinases with the claimed compounds. The "how to use" requirements of 35 USC 112 are not met by disclosing only a pharmacological activity of the claimed compounds if one skilled in the art would not be able to use the compounds effectively without undue experimentation. See **In re Diedrich**, 138 USPQ 128; **In re Gardner et. al.**, 166 USPQ 138. Thus, where the claimed compounds do not bear structures that are similar to known compounds having the same activity, and their pharmaceutical properties could not be predicted from their chemical structure, a disclosure that they possess a particular activity may not suffice as a description of how to use as required by 35 USC 112. See **In re Moureu et. al**. 145 USPQ 452.